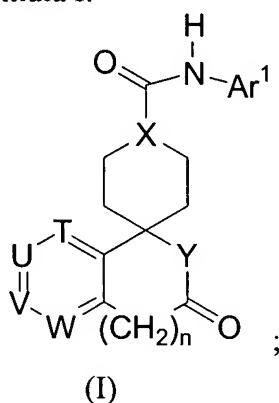


IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Cancel Claims 1-55

56. (new) A composition comprising
(a) a NPY5 antagonist of formula I:



and pharmaceutically acceptable salts and esters thereof, wherein
Ar¹ is selected from the group consisting of:

- (1) aryl, and
- (2) heteroaryl,

wherein the aryl and heteroaryl groups are unsubstituted or optionally substituted with a substituent selected from the group consisting of:

- (a) halogen,
- (b) nitro,
- (c) lower alkyl,
- (d) halo(lower)alkyl,
- (e) hydroxy(lower)alkyl,
- (f) cyclo(lower)alkyl,
- (g) lower alkenyl,
- (h) lower alkoxy,
- (i) halo(lower)alkoxy,
- (j) lower alkylthio,
- (k) carboxyl,

- (l) lower alkanoyl,
- (m) lower alkoxy carbonyl,
- (n) lower alkylene optionally substituted with oxo, and
- (o) -Q-Ar²;

Ar² is selected from the group consisting of

- (1) aryl, and
- (2) heteroaryl,

wherein aryl and heteroaryl are unsubstituted or optionally substituted with a substituent selected from the group consisting of:

- (a) halogen,
- (b) cyano,
- (c) lower alkyl,
- (d) halo(lower)alkyl,
- (e) hydroxy(lower)alkyl,
- (f) hydroxy,
- (g) lower alkoxy,
- (h) halo(lower)alkoxy,
- (i) lower alkylamino,
- (j) di-lower alkylamino,
- (k) lower alkanoyl, and
- (l) aryl;

n is 0 or 1;

Q is selected from the group consisting of a single bond or carbonyl;

T, U, V and W are each independently selected from the group consisting of

- (1) nitrogen, and
- (2) methine,

wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy, and

wherein at least two of T, U, V, and W are methine;

X is selected from the group consisting of

- (1) nitrogen, and
- (2) methine; and

Y is selected from the group consisting of

- (1) imino, unsubstituted or optionally substituted with lower alkyl, and
- (2) oxygen; and

(b) an anti-obesity agent selected from the group consisting of: a NPY1 antagonist, or a pharmaceutically acceptable salt or ester thereof.

57. (new) The composition of Claim 56 wherein the NPY1 antagonist is selected from the group consisting of: J-115,814, or a pharmaceutically acceptable salt or ester thereof.

58. (new) The composition of Claim 56 wherein the NPY5 antagonist is selected from the group consisting of

- (1) 3-oxo-N-(5-phenyl-2-pyrazinyl)-spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide;
- (2) 3-oxo-N-(7-trifluoromethylpyrido[3,2-b]pyridin-2-yl)spiro-[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide;
- (3) N-[5-(3-fluorophenyl)-2-pyrimidinyl]-3-oxospiro-[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide;
- (4) trans-3'-oxo-N-(5-phenyl-2-pyrimidinyl)spiro[cyclohexane-1,1'(3'H)-isobenzofuran]-4-carboxamide;
- (5) trans-3'-oxo-N-[1-(3-quinolyl)-4-imidazolyl]spiro[cyclohexane-1,1'(3'H)-isobenzofuran]-4-carboxamide;
- (6) trans-3-oxo-N-(5-phenyl-2-pyrazinyl)spiro[4-azaiso-benzofuran-1(3H),1'-cyclohexane]-4'-carboxamide;
- (7) trans-N-[5-(3-fluorophenyl)-2-pyrimidinyl]-3-oxospiro[5-azaisobenzofuran-1(3H),1'-cyclohexane]-4'-carboxamide;
- (8) trans-N-[5-(2-fluorophenyl)-2-pyrimidinyl]-3-oxospiro[5-azaisobenzofuran-1(3H),1'-cyclohexane]-4'-carboxamide;
- (9) trans-N-[1-(3,5-difluorophenyl)-4-imidazolyl]-3-oxospiro[7-azaisobenzofuran-1(3H),1'-cyclohexane]-4'-carboxamide;
- (10) trans-3-oxo-N-(1-phenyl-4-pyrazolyl)spiro[4-azaisobenzofuran-1(3H),1'-cyclohexane]-4'-carboxamide;

(11) trans-N-[1-(2-fluorophenyl)-3-pyrazolyl]-3-oxospiro[6-azaisobenzofuran-1(3H),1'-cyclohexane]-4'-carboxamide;

(12) trans-3-oxo-N-(1-phenyl-3-pyrazolyl)spiro[6-azaisobenzofuran-1(3H),1'-cyclohexane]-4'-carboxamide; and

(13) trans-3-oxo-N-(2-phenyl-1,2,3-triazol-4-yl)spiro[6-azaisobenzofuran-1(3H),1'-cyclohexane]-4'-carboxamide;

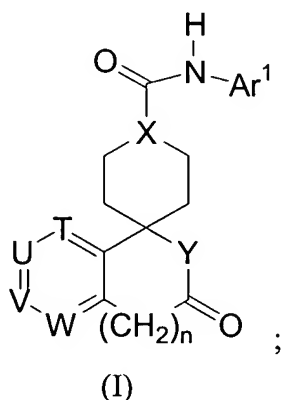
and pharmaceutically acceptable salts and esters thereof.

59. (new) The composition of Claim 58 wherein the NPY5 antagonist is selected from the group consisting of: 3-oxo-N-(5-phenyl-2-pyrazinyl)-spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, or a pharmaceutically acceptable salt or ester thereof.

60. (new) A composition according to Claim 1 further comprising a pharmaceutically acceptable carrier.

61. (new) A method of preventing obesity in a subject at risk for obesity comprising administration to said subject

(a) a prophylactically effective amount of a NPY5 antagonist of Formula I:



and pharmaceutically acceptable salts and esters thereof, wherein

Ar¹ is selected from the group consisting of:

- (1) aryl, and
- (2) heteroaryl,

wherein the aryl and heteroaryl groups are unsubstituted or optionally substituted with a substituent selected from the group consisting of:

- (a) halogen,
- (b) nitro,

- (c) lower alkyl,
- (d) halo(lower)alkyl,
- (e) hydroxy(lower)alkyl,
- (f) cyclo(lower)alkyl,
- (g) lower alkenyl,
- (h) lower alkoxy,
- (i) halo(lower)alkoxy,
- (j) lower alkylthio,
- (k) carboxyl,
- (l) lower alkanoyl,
- (m) lower alkoxycarbonyl,
- (n) lower alkylene optionally substituted with oxo, and
- (o) -Q-Ar²;

Ar² is selected from the group consisting of

- (1) aryl, and
- (2) heteroaryl,

wherein aryl and heteroaryl are unsubstituted or optionally substituted with a substituent selected from the group consisting of:

- (a) halogen,
- (b) cyano,
- (c) lower alkyl,
- (d) halo(lower)alkyl,
- (e) hydroxy(lower)alkyl,
- (f) hydroxy,
- (g) lower alkoxy,
- (h) halo(lower)alkoxy,
- (i) lower alkylamino,
- (j) di-lower alkylamino,
- (k) lower alkanoyl, and
- (l) aryl;

n is 0 or 1;

Q is selected from the group consisting of a single bond or carbonyl;

T, U, V and W are each independently selected from the group consisting of

- (1) nitrogen, and

(2) methine,

wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy, and

wherein at least two of T, U, V, and W are methine;

X is selected from the group consisting of

- (1) nitrogen, and
- (2) methine; and

Y is selected from the group consisting of

- (1) imino, unsubstituted or optionally substituted with lower alkyl, and
- (2) oxygen; and

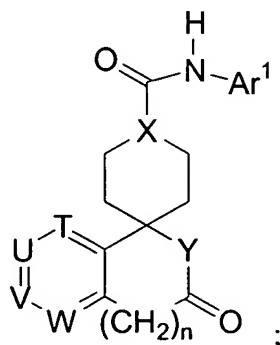
(b) a prophylactically effective amount of an anti-obesity agent selected from the group consisting of: a NPY1 antagonist, or a pharmaceutically acceptable salt or ester thereof.

62. (new) The method of Claim 61 wherein the NPY1 antagonist is selected from the group consisting of: J-115,814, or a pharmaceutically acceptable salt or ester thereof.

63. (new) The method of Claim 61 wherein the NPY5 antagonist is selected from the group consisting of: 3-oxo-N-(5-phenyl-2-pyrazinyl)-spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, or a pharmaceutically acceptable salt or ester thereof.

64. (new) A method of treating a subject having a disorder associated with excessive food intake comprising administration of

(a) a therapeutically effective amount of a NPY5 antagonist of Formula I:



(I)

and pharmaceutically acceptable salts and esters thereof, wherein

Ar¹ is selected from the group consisting of:

- (1) aryl, and
- (2) heteroaryl,

wherein the aryl and heteroaryl groups are unsubstituted or optionally substituted with a substituent selected from the group consisting of:

- (a) halogen,
- (b) nitro,
- (c) lower alkyl,
- (d) halo(lower)alkyl,
- (e) hydroxy(lower)alkyl,
- (f) cyclo(lower)alkyl,
- (g) lower alkenyl,
- (h) lower alkoxy,
- (i) halo(lower)alkoxy,
- (j) lower alkylthio,
- (k) carboxyl,
- (l) lower alkanoyl,
- (m) lower alkoxycarbonyl,
- (n) lower alkylene optionally substituted with oxo, and
- (o) -Q-Ar²;

Ar² is selected from the group consisting of

- (1) aryl, and
- (2) heteroaryl,

wherein aryl and heteroaryl are unsubstituted or optionally substituted with a substituent selected from the group consisting of:

- (a) halogen,
- (b) cyano,
- (c) lower alkyl,
- (d) halo(lower)alkyl,
- (e) hydroxy(lower)alkyl,
- (f) hydroxy,
- (g) lower alkoxy,

- (h) halo(lower)alkoxy,
- (i) lower alkylamino,
- (j) di-lower alkylamino,
- (k) lower alkanoyl, and
- (l) aryl;

n is 0 or 1;

Q is selected from the group consisting of a single bond or carbonyl;

T, U, V and W are each independently selected from the group consisting of

- (1) nitrogen, and
- (2) methine,

wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy, and

wherein at least two of T, U, V, and W are methine;

X is selected from the group consisting of

- (1) nitrogen, and
- (2) methine; and

Y is selected from the group consisting of

- (1) imino, unsubstituted or optionally substituted with lower alkyl, and
- (2) oxygen; and

(b) a therapeutically effective amount of an anti-obesity agent selected from the group consisting of: a NPY1 antagonist, or a pharmaceutically acceptable salt or ester thereof, to a subject in need of such treatment.

65. (new) The method of Claim 64 wherein the NPY1 antagonist is selected from the group consisting of: J-115,814, or a pharmaceutically acceptable salt or ester thereof.

66. (new) The method of Claim 64 wherein the NPY5 antagonist is selected from the group consisting of: 3-oxo-N-(5-phenyl-2-pyrazinyl)-spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, or a pharmaceutically acceptable salt or ester thereof.

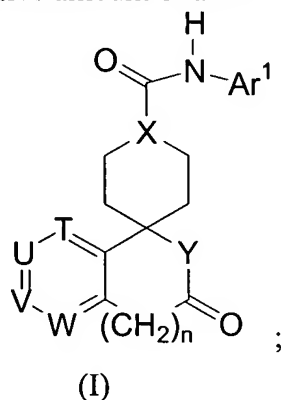
67. (new) The method according to Claim 64 wherein the disorder associated with excessive food intake is selected from obesity and an obesity-related disorder.

68. (new) The method according to Claim 67 wherein the obesity-related disorder is selected from: overeating; bulimia; hypertension; diabetes, elevated plasma insulin concentrations; insulin resistance; dyslipidemia; hyperlipidemia; endometrial, breast, prostate and colon cancer; osteoarthritis; obstructive sleep apnea; cholelithiasis; gallstones; coronary heart disease; abnormal heart rhythms; heart arrhythmias; myocardial infarction; polycystic ovarian disease; craniopharyngioma; the Prader-Willi Syndrome; Frohlich's syndrome; GH-deficient subjects; normal variant short stature; Turner's syndrome; and acute lymphoblastic leukemia.

69. (new) The method according to Claim 67 wherein the obesity-related disorder is diabetes.

70. (new) A method of maintaining weight loss in a subject comprising administration of

(a) a therapeutically effective amount of a NPY5 antagonist of Formula I:



and pharmaceutically acceptable salts and esters thereof, wherein Ar¹ is selected from the group consisting of:

- (1) aryl, and
- (2) heteroaryl,

wherein the aryl and heteroaryl groups are unsubstituted or optionally substituted with a substituent selected from the group consisting of:

- (a) halogen,
- (b) nitro,

- (c) lower alkyl,
- (d) halo(lower)alkyl,
- (e) hydroxy(lower)alkyl,
- (f) cyclo(lower)alkyl,
- (g) lower alkenyl,
- (h) lower alkoxy,
- (i) halo(lower)alkoxy,
- (j) lower alkylthio,
- (k) carboxyl,
- (l) lower alkanoyl,
- (m) lower alkoxycarbonyl,
- (n) lower alkylene optionally substituted with oxo, and
- (o) -Q-Ar²;

Ar² is selected from the group consisting of

- (1) aryl, and
- (2) heteroaryl,

wherein aryl and heteroaryl are unsubstituted or optionally substituted with a substituent selected from the group consisting of:

- (a) halogen,
- (b) cyano,
- (c) lower alkyl,
- (d) halo(lower)alkyl,
- (e) hydroxy(lower)alkyl,
- (f) hydroxy,
- (g) lower alkoxy,
- (h) halo(lower)alkoxy,
- (i) lower alkylamino,
- (j) di-lower alkylamino,
- (k) lower alkanoyl, and
- (l) aryl;

n is 0 or 1;

Q is selected from the group consisting of a single bond or carbonyl;

T, U, V and W are each independently selected from the group consisting of

(1) nitrogen, and

(2) methine,

wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

(a) halogen,

(b) lower alkyl,

(c) hydroxy, and

(d) lower alkoxy, and

wherein at least two of T, U, V, and W are methine;

X is selected from the group consisting of

(1) nitrogen, and

(2) methine; and

Y is selected from the group consisting of

(1) imino, unsubstituted or optionally substituted with lower alkyl, and

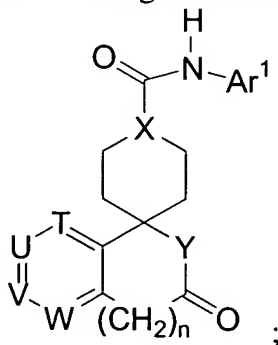
(2) oxygen; and

(b) a therapeutically effective amount of an anti-obesity agent selected from the group consisting of: a NPY1 antagonist, or a pharmaceutically acceptable salt or ester thereof, to a subject in need of such treatment.

71. (new) The method of Claim 70 wherein the NPY1 antagonist is selected from the group consisting of: J-115,814, or a pharmaceutically acceptable salt or ester thereof.

72. (new) The method of Claim 71 wherein the NPY5 antagonist is selected from the group consisting of: 3-oxo-N-(5-phenyl-2-pyrazinyl)-spiro[isobenzofuran-1(3H),4'-piperidine]-1'-carboxamide, or a pharmaceutically acceptable salt or ester thereof.

73. (new) A kit comprising at least one unit dosage of a prophylactically or therapeutically effective amount of a NPY5 antagonist of Formula I:



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(I)

and pharmaceutically acceptable salts and esters thereof, and at least one unit dosage of a prophylactically or therapeutically effective amount of a NPY1 antagonist, or a pharmaceutically acceptable salt or ester thereof.